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## REMARKS

### Pending Claims and Preliminary Amendment

In the Office Action of July 2, 2004, it is stated that only claims 1-16 are pending. This is incorrect. On March 11, 2002, Applicants filed a Preliminary Amendment in which claims 1 and 3-16 were amended and new claims 17-20 were added. These new claims are directed to synthetic melanins and thus Applicants assume they will be grouped with Group I.

A copy of the March 11, 2002, Preliminary Amendment and the stamped receipt postcard are enclosed for the Examiner's convenience.

### Election

In response to the Restriction Requirement, Applicants hereby elect Group I, claims 1-56, drawn to synthetic melanins. However, the Restriction is respectfully traversed.

The sole basis for the Restriction is the unsubstantial argument that Group I claims are anticipated by DE 197 17 837, WO 96/25920 or JP 03-077813. This allegation is unsubstantiated since it does not set forth where each of these references discloses each of the features of claim 1. In making an anticipation rejection, an examiner must show where each and every feature of the claimed invention is described in the allegedly anticipatory reference. See, e.g., *Ex parte Levy*, 17 USPQ2d 1461, 1462 (BOPA 1990) [“Moreover, it is incumbent upon the Examiner to identify wherein each and every facet of the claimed invention is disclosed in the applied reference. ”].

Moreover, if this bare allegation were sufficient, then all an Examiner would need to assert to justify a Restriction would be to allege that a claim was unpatentable over any piece of prior art. Such practice is not sanctioned by any section of the MPEP.

Moreover, upon demonstrating that claim 1 is patentable over the prior art, based on arguments and/or amendments, the sole basis for the Restriction would be eliminated. Thus, rejoinder of the non-elected claims would be proper.

With respect to PCT Rule 13.2, all of the claims refer to the melanin of claim 1. Thus, all of the claims contain the special technical feature(s) as recited in claim 1. Unity is present. See, e.g., examples 1 of Annex B of the PCT Rules. In this example, the claims are

directed to substance X, a method of making substance X, and a use of substance X. Since all of these contain the special common technical feature, i.e., substance X, unity exists.

Thus, withdrawal of the Restriction is respectfully requested. If not withdrawn, Applicants will request rejoinder once claim 1 is determined to be allowable.

In response to the Election of Species Requirement, with respect to component "B" Applicants are unsure whether the election requires selection from each of subsection (i)-(iii) or from just one of them. Clarification is requested.

If the Election requires selection from each of subsections (i)-(iii) of component B, then Applicants elect the following species:

Component A: a monomer unit of a plant phenol and an eumelanin;

Component B(i): OPC;

Component B(ii): a mixture of cyanidin and delphinidin;

Component B(iii): gallic acid;

Component C: L-dopa;

Component D: laccases;

Component E: the plant monomer unit.

If the Election requires selection from only one of subsections (i)-(iii) of component B, then Applicants elect the following species:

Component A: a monomer unit of a plant phenol and an eumelanin;

Component B(i): OPC;

Component C: L-dopa;

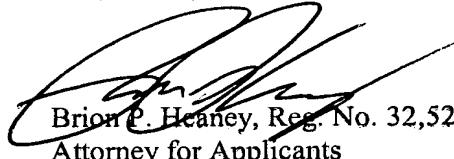
Component D: laccases;

Component E: the plant monomer unit.

It is Applicants' understanding that, following this election, examination will proceed in accordance with MPEP §809.02(c). In particular, it is Applicants understanding upon determination that the elected species is allowable, the examination will be extended to other species and further, upon determination that a generic claim is allowable, Applicants will be advised that the claims drawn to the non-elected species are no longer withdrawn. See MPEP §809.02(c)(B)(1).

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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BPH

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**U.S. NATIONAL PHASE APPLICATION CORRESPONDING  
TO PCT/IB00/01276 FILED 8 SEPTEMBER 2000**

APPLICANT(S): GHISALBERTI, Carlo

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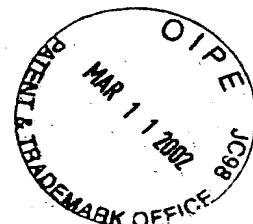
U.S. NATIONAL PHASE DEPOSITED: 7 MARCH 2002

TITLE: SYNTHETIC VEGETAL MELANINS, PROCESS FOR THEIR PRODUCTION AND COMPOSITIONS  
CONTAINING THEREOF

THE PATENT AND TRADEMARK OFFICE STAMP HEREON ACKNOWLEDGES  
RECEIPT OF THE FOLLOWING PAPERS:

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FEES \$ \_\_\_\_\_ Check No. \_\_\_\_\_  
 TRANSMITTAL LETTER  
 PRELIMINARY AMENDMENT  
 DECLARATION  
 APPLICATION DATA SHEET  
 ASSIGNMENT WITH RECORDATION COVER SHEET AND CK. NO. FOR \$ \_\_\_\_\_  
 TOTAL PAPERS OF APPLICATION: 43, INCLUDING SPECIFICATION 32 PGS.; CLAIMS 3 PGS.;  
ABSTRACT 1 PGS; DRAWINGS 6 PGS.; FACE PAGE OF PUBLICATION, INCLUDING ABSTRACT (1 PGS.);  
TRANSLATION OF PUBLICATION COVER SHEETS, INCLUDING ABSTRACT PGS.  
 TRANSLATION OF ANNEXES OF IPER



OTHER \_\_\_\_\_

Initials: IWM:kmo.

Date Filed: 7 March 2002

*PRCT 3/11/02-1F*



IN THE UNITED STATES DESIGNATED/ELECTED OFFICE

International Application No. : PCT/IB00/01276

International Filing Date : 8 SEPTEMBER 2000

Priority Date(s) Claimed : 9 SEPTEMBER 1999

Applicant(s) (DO/EO/US) : GHISALBERTI, Carlo

Title: SYNTHETIC VEGETAL MELANINS, PROCESS FOR THEIR PRODUCTION AND COMPOSITIONS  
CONTAINING THEREOF

PRELIMINARY AMENDMENT

Commissioner for Patents  
Washington, D.C. 20231

SIR:

Prior to calculating the national fee, and prior to examination in the National Phase of the above-identified International application, please amend as follows:

IN THE CLAIMS:

1. (Amended) Synthetic vegetal melanins obtainable by in vitro polymerization of at least one monomer unit (a), and optionally at least one compound (b), wherein:
  - (a) is a plant polyphenol; and
  - (b) is an eumelanin precursor;said synthetic vegetal melanin being characterized by a Red:Green:Blue ratio comprised between 1 : 0.88 : 0.84 and 1 : 0.64 : 0.41.
3. (Amended) Synthetic vegetal melanins according to claim 2, wherein the plant polyphenol of formula (I) with X being a residue of formula (II) is a flavonoid selected from the group consisting of quercetin, fisetin, fustin, luteolin, OPC, catechin, epicatechin, GC, GCG, EGC,EGCG, myricetin, dihydroquercetin and mixtures thereof.

4. (Amended) Synthetic vegetal melanins according to claim 2, wherein the plant polyphenol of formula (I) with X being a residue of formula (III) is a flavonoid anthocyanins selected from the group consisting of cyanidin, delphinidin and mixtures thereof.

5. (Amended) Synthetic vegetal melanins according to claim 2, wherein the plant polyphenol of formula (I) with X being a residue of formula (IV) is an open ring dihydroxyphenol selected from the group consisting of hydroxytyrosol, protocathechuic acid, protocathechuic aldehyde, gallic acid, tannic acid and mixtures thereof.

6. (Amended) Synthetic vegetal melanins according to claim 1, comprising said eumelanin precursor wherein the eumelanin precursor is selected from the group consisting of L-dopa, DHI, DHICA, dopamine, pyrocatechol, pyrogallol and mixtures thereof.

7. (Amended) A method of producing synthetic vegetal melanins according to claim 1 comprising bubbling air or oxygen through an alkaline aqueous solution comprising the at least one monomer at a pH of at least 10, during 12 to 48 hours, at a temperature ranging from 10 to 90°C.

8. (Amended) A method of claim 7, send alkaline aqueous solution further comprising catalytic amounts of pro-oxidant metals selected from the group consisting of Cu<sup>++</sup>, Fe<sup>++</sup>, Ni<sup>++</sup>, Co<sup>++</sup> and mixtures thereof.

9. (Amended) A method of producing synthetic vegetal melanins according to claim 1 comprising polymerizing at the least one monomer with a chemical oxidizing agent selected from the group consisting of hydrogen peroxide, hydrogen iodide, ammonium persulfate, potassium permanganate, magnesium perchlorate and mixtures thereof.

10. (Amended) A method of producing synthetic vegetal melanins according to claim 1 comprising bubbling air or oxygen through an buffered aqueous solution comprising the at least one monomer at a pH from 9.5 to 4.5, during 12 to 48 hours, at a temperature ranging from 20 to 45°C in presence of a melanin-forming enzyme.

11. (Amended) Method of claim 10, wherein the enzyme is selected from the group consisting of tyrosinases, polyphenoloxidases (catachol oxidases), phenolases, (phenoloxidases), peroxidases, laccases, lipoxygenase, and mixtures thereof.

12. (Amended) A method according to claim 10 wherein the monomer units (a) or(b) are formed in situ from pre-momomers, bearing a monophenolic moiety.

13. (Amended) A method of claim 12 where the pre-momomers are selected from the group consisting of dihydrokaempferol, armadendrin, p-hydroxybenzaldehyde, PHBA, tyrosol, p-coumaric acid, apigenin, kaempferol, pelargonin, genistein, tyrosine, tyramine, 5-hydroxy-indole and mixtures thereof.

14. (Amended) A cosmetic composition comprising as active ingredient at least one synthetic vegetal melanins according to claim 1.

15. (Amended) A cosmetic composition according to claim 14, including additives for facial make-up, hair dyes, tanning, anti-sun, toiletry, or for moisturizing and protective skin.

16. (Amended) A pharmaceutical or nutritional composition having anti-inflammatory and immunomodulation activity which comprises as active ingredient at least a synthetic vegetal melanin according to claim 1.

PLEASE ADD THE FOLLOWING NEW CLAIMS:

17.(Amended) Synthetic vegetal melanins according to claim 2, comprising said eumelanin precursor wherein the eumelanin precursor is selected from the group consisting of L-dopa, DHI, DHICA, dopamine, pyrocatechol, pyrogallol and mixtures thereof.

18.(Amended) Synthetic vegetal melanins according to claim 3, comprising said eumelanin precursor wherein the eumelanin precursor is selected from the group consisting of L-dopa, DHI, DHICA, dopamine, pyrocatechol, pyrogallol and mixtures thereof.

19.(Amended) Synthetic vegetal melanins according to claim 4, comprising said eumelanin precursor wherein the eumelanin precursor is selected from the group consisting of L-dopa, DHI, DHICA, dopamine, pyrocatechol, pyrogallol and mixtures thereof.

20.(Amended) Synthetic vegetal melanins according to claim 5, comprising said eumelanin precursor wherein the eumelanin precursor is selected from the group consisting of L-dopa, DHI, DHICA, dopamine, pyrocatechol, pyrogallol and mixtures thereof.

REMARKS

The purpose of this Preliminary Amendment is to eliminate multiple dependent claims in order to avoid the additional fee. Applicants reserve the right to reintroduce claims to canceled combined subject matter.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**Version With Markings to Show Changes Made**".

Respectfully submitted,



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IWM:kmo

Filed: 11 MARCH 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 1 and 3 to 17 were amended as follows:

1. (Amended) Synthetic vegetal melanins obtainable by in vitro polymerization of at least one monomer unit (a), and optionally at least one compound (b), wherein:
  - (a) is a plant polyphenol; and
  - (b) is an eumelanin precursors;  
said synthetic vegetal melanin being characterized by a Red:Green:Blue ratio comprised between 1 : 0.88 : 0.84 and 1 : 0.64 : 0.41.
3. (Amended) Synthetic vegetal melanins according to claims 1 to claim 2, wherein the plant polyphenol of formula (I) with X being a residue of formula (II) is a flavonoid selected infrom the group consisting inof quercetin, fisetin, fustin, luteolin, OPC, catechin, epicatechin, GC, GCG, EGC,EGCG, myricetin, dihydroquercetin and mixturesof thereof.
4. (Amended) Sythetic vegetal melanins according to claims 1 to claim 2, wherein the plant polyphenol of formula (I) with X being a residue of formula (III) is a flavonoid anthocyanins selected infrom the group consisting inof cyanidin, delphinidin and mixturesof thereof.
5. (Amended) Synthetic vegetal melanins according to claims 1 to 2, wherein the plant polyphenol of formula (I) with X being a residue of formula (IV) is an open ring dihydroxyphenol selected infrom the group consisting inof hydroxytyrosol, protocathechuic acid, protocathechuic aldehyde, gallic acid, tannic acid and mixturesof thereof.
6. (Amended) Synthetic vegetal melanins according to claims 1 to 2, comprising said eumelanin precursor wherein the eumelanin precursor is selected infrom the group consisting inof L-dopa, DHI, DHICA, dopamine, pyrocatechol, pyrogallol and mixturesof thereof.

7. ~~M~~(Amended) A method of producing synthetic vegetal melanins according to claims 1 to 6 comprising bubbling air or oxygen through an alkaline aqueous solution ~~of~~comprising the at least one monomers at a pH ~~of at least 10 or higher~~, during 12 to 48 hours, at a temperature ranging from 10 to 90°C.

8. ~~M~~(Amended) A method of claim 7, ~~send~~ alkaline aqueous solution further comprising catalytic amounts of pro-oxidant metals selected ~~in~~from the group consisting ~~in~~of Cu<sup>++</sup>, Fe<sup>++</sup>, Ni<sup>++</sup>, Co<sup>++</sup> and mixture thereof.

9. (Amended) A method of producing synthetic vegetal melanins according to claim 1 comprising polymerizing at the least one monomer with a chemical oxidizing agent is selected ~~in~~from the group consisting ~~in~~of hydrogen peroxide, hydrogen iodide, ammonium persulfate, potassium permanganate, magnesium perchlorate and mixtures thereof.

10. ~~M~~(Amended) A method of producing synthetic vegetal melanins according to claim 1 to 6 comprising bubbling air or oxygen through an buffered aqueous solution ~~of~~comprising the at least one monomers at a pH from 9.5 to 4.5, during 12 to 48 hours, at a temperature ranging from 20 to 45°C in presence of a suitable ~~melanin-forming~~ enzyme.

11. (Amended) Method of claim 10, wherein the enzyme is selected ~~in~~from the group consisting ~~in~~of tyrosinases, polyphenoloxidases (catachol oxidases), phenolases, (phenoloxidases), peroxidases, laccases, lypooxygenase, and mixtures thereof.

12. ~~M~~(Amended) A method according to claims 10 to 12 wherein the monomer units (a) or(b) are formed in situ from pre-momomers, bearing a monophenolic moiety.

13. ~~M~~(Amended) A method of claim 12 where the pre-momomers are selected ~~in~~from the group consisting ~~in~~of dihydrokaempferol, armadendrin, p-hydroxybenzaldehyde, PHBA, tyrosol, p-coumaric acid, apigenin, kaempferol, pelargonin, genistein, tyrosine, tyramine, 5-hydroxy-indole and mixtures thereof.

14. ~~E~~(Amended) A cosmetic composition comprising as active ingredient at least one synthetic vegetal melanins according to claims 1 to 6.

15. ~~E~~(Amended) A cosmetic composition according to claim 14, including additives for facial make-up, hair dyes, tanning, anti-sun, toiletry, or for moisturizing and protective skin.

16. ~~Pharmaceutical~~(Amended) A pharmaceutical or nutritional composition having anti-inflammatory and immunomodulation activity which comprises as active ingredient at least a synthetic vegetal melanin according to claims 1 to 6.

Claims 17 to 20 were newly added.